
Domenico Mazzone, Laura Battaglia, Luigi Mazzone, Francesca Andreozzi, Maria Antonietta Romeo

Division of Child Neurology and Psychiatry
Department of Pediatrics, University of Catania, Catania Italy

Corresponding author:
Domenico Mazzone, M.D.
University of Catania
Department of Pediatrics
Division of Child Neurology and Psychiatry

Address:
Via S. Sofia, 78
Zip Code: 95123
Catania (Italy)

Telephone number:
011 39 095-3782436
Fax (+39) 095-222532
e-mail: mazzone@unict.it
Background and objective.

Familiar Cognitive-behavioural therapy (FCBT) can be an useful psychological approach for β-thalassaemia major, increasing compliance to treatment and improving the emotional burden of disease.

Design and methods

Following FCBT lasting 1 year, 28 β-thalassaemic major children were assessed about compliance to chelation, behavioural, mood and temperamental characteristics in comparison with healthy children. Mothers were investigated about quality of life.

Results

90% of patients had good compliance to chelation therapy, however somatic complaints, physical symptoms and separation panic were relevant among the patients, scoring higher than control group; temperamental evaluation revealed high emotionality and poor sociability in patients and mothers. Impairment on physical and psychological health, quality of life and general health domains was evident in mothers of patients.

Interpretation and conclusion

FCBT is a valid tool to increase compliance to chelation, however not fully effective to reduce anxiety in β-thalassaemic children nor to improve quality of life of caregiving mothers.

Key Words: β-Thalassaemia, Children, Anxiety disorders, Familiar Cognitive-behavioural therapy, Quality of life.
Introduction

β−Thalassemia major is an hereditary disorder characterized by defective production of hemoglobin, and excessive destruction of red blood cells, common treatment is blood transfusion and iron chelation. Children can manifest fear for possible complications, emotional burden, hopelessness, difficulty on social integration; they can have impaired abstract reasoning, deficits of language, attention, memory, constructional/visual spatial skills and executive functions, that are more prominent in hemosiderotic subjects. 1

The intelligence quotient appears uncorrelated to age, sex, ferritin level, brainstem auditory, visual and somatosensory evoked potentials, motor and sensory nerve conduction velocity, rather to poor school performances and physical or social restrictions for the severity and chronicity of the disease. 2,3

Behavioural characteristics of patients are seen similar to normal peers, however many patients show severe psychosocial problems for difficulty to comply with the painful chelation; male patients, also, can manifest oppositional defiant disorders. 4,5,6

Most children feel themselves different from their peers and elaborate negative thoughts about their life, guilt senses, increased anxiety and low self-esteem; in addition, the chronic course of illness can cause in the families altered relationships between members, marginalization and isolation.

As a chronic disease with a considerable role for self-management, psychological support seems appropriate for managing thalassaemia as it could improve the compliance and reduce the emotional impact. Significantly higher psychosocial morbidity and psychosocial aspects, in fact, need to be addressed in the overall treatment of children with thalassaemia to prevent the development of clinically manifest psychological disease. 7

In present study we have given a psychological support to β-thalassaemia major children by Familiar Cognitive-behavioural therapy (FCBT) for 1 year, with aim to improve their adherence to life-long
iron chelation and reduce emotional burden; we have included caregiving mothers in FBCT sessions as maternal participation could be an useful strategy for prevention or treatment of anxiety in children.

After FBCT β-thalassaemia major children have been evaluated about compliance to chelation and assessed on behaviour, mood, and temperamental charactereristics.

Additional goal of study was to analyze quality of life (QoL) of caregiving mothers, that taking on a considerable part of medical care might be affected in some domain.

**Sample and methods**

28 outpatients meeting the diagnostic criteria for β-thalassaemia major aged 12.79±3.57 years (n. 15 13 years) were submitted to FBCT (2 x weekly 45-min sessions) for 1 year; their mothers participated to sessions collaborating with the psychologist (F.A.).

28 healthy subjects aged 12.52±3.48 years (n.14 > 13 years) were randomly enrolled from a database of children attending a well-being paediatric clinic for routine checks.

Two groups were similar for sex, socio-economic status and education.

Diagnosis of β-thalassaemia major was made in each patient before 3 years of age and parents received adequate informations about treatment, prognosis and inheritance.

High haemo-transfusional regimen was carried out and chelation with Desferioxamine was performed by subcutaneous infusion 10-12 hours a day for 5-6 days a week (25-50 mg/kg). No family history of psychological illness was noticed.

After 1 year of FBCT, β-thalassaemia major children were evaluated about compliance index (as percentage), calculated by relationship between days of administration of therapy and days of prescription within the last 1 year; an index > 75% indicated a good compliance.

Physical, neurological, ophtalmologic examination and e.e.g. were performed.

All participants were submitted to following psychological instruments for comprehensive evaluation of behaviour, mood, and temperament and compared to healthy subjects:

a) Wechsler Intelligence Scale for Children (WISC-IV) for the intelligence quotient (I.Q.).

b) Child Behaviour Checklist (CBCL), completed by the parents rating behavioural and emotional
problems along two dimensions of ‘internalizing’ symptoms such as anxiety and depression, and ‘externalising’ symptoms, such as aggression and hyperactivity. Raw score of each clinical factor was transformed to T scores based on published norms. 10.

c) Multidimensional Anxiety Scale for Children (MASC), completed by the child to score symptoms of anxiety according to 4-point Likert-style self-report scale. Subfactors include physical symptoms, harm avoidance, social anxiety, and separation anxiety. The raw score was converted into standard T-scores. 11.

d) Children’s Depression Inventory (CDI), completed by the child to rate symptoms of depression. The CDI is a self-rating scale scored on three-point scale (0 absent; 1 moderate; 2 severe) reflecting growing severity of symptoms. Total score ranges from 0 to 54; 19-point cut-off indicates the threshold discriminating children at risk of depression. 12.

e) EAS Scale was administered to children and their caregiving mothers to rate four temperamental traits: Emotionality, Activity, Sociability, and Shyness. For each one it was asked to rate the statement on a “5 point” Likert scale, ranging from 0 (not characteristic or typical) to 5 (very characteristic or typical). 13.

f) WHOQOL-Bref questionnaire was administered to mothers of β-thalassaemia major children and mothers of normal subjects. It has 26 items and four domains related to quality of life: physical health, psychological health, social relationships and environment, and two individual items covering overall quality of life and general health. Higher scores denote better QOL. 14.

The WHOQOL-Bref domain scores showed good discriminant validity and internal consistency of subscales evaluated by Cronbach’s alpha coefficients (alpha P≥0.75).

Data were analysed with standard descriptive statistics: χ² test, Mann-Whitney U test. A two-tail P value of < .05 was used as the cut-off point of statistical significance.

Informed consent was obtained from children and their mothers.

**Results**

β-thalassaemia major children and control subjects had not physical, neurological, ophtalmological
and e.g. anomaly.

Mean age, males/females ratio and I.Q. were similar in the two groups.

Compliance to treatment of β-thalassaemic children was good in 25/28 patients, greater than 90% (P<.000).

Compared to healthy subjects, β-thalassaemic children at CBCL scored more for Somatic complaints (58.29±7.37 vs. 53.32±4.48, p<.005) and at MASC for Physical symptoms (48.79±6.37 vs. 45.04±3.52, p<.005) and Separation panic (53.36±10.31 vs. 48.18±6.96, p<.05).

At EAS, patients displayed high emotionality (p < .05) and low sociability (p < .000); their mothers, also, high emotionality and shyness, and low sociability.

CDI scores were not different in β-thalassaemic children and in healthy subjects, however in 3 patients scores exceeded the cut-off.

At WHOQOL-Bref questionnaire mothers of β-thalassaemic children showed impairment in the following domains: Physical health, Psychological health, quality of life and general health.

Data are reported in tables 1-3.

**Discussion**

Beta-Thalassaemia is a chronic illness that causes excessive psychological burden to children and their families as clinical manifestations usually develop early in the life and invasive procedures induce a remarkable suffering. 15

Experience using continuous Desferoxamine infusion demonstrated that local reactions could result in inadequate compliance in many patients, higher morbidity, and increased costs. 16.

High levels of anxiety have also been consistent features of studies of psychosocial dysfunction in thalassaemic patients and their parents. 17.

90% of our β-thalassaemic major children had good compliance, suggesting FCBT was effective for this purpose, however Somatic complaints (at CBCL), Physical Symptoms and Separation Panic (at MASC) resulted with higher scores could suggesting persistently emotional burden.
Therefore, FCBT could be considered appropriate approach because closer to treatment of psychological comprehensive disorders, however its role is controversial for preventing different aspects of anxiety.

Temperamental background could influence personality, as EAS indicated higher emotionality and reduced sociability in children and higher emotionality, shiness and lower sociability in their mothers, suggesting behavioural inhibition of mothers and offsprings.

CDI, an instrument designed to measure self-rated assessment of self-reported key symptoms of lowered mood did not show, instead, any relevant anomaly in β-thalassemic children.

Evaluation of QoL of caregivers was additional goal of present study.

We have found a significant impairment in mothers of β-thalasaemic children on Physical health (concerning energy and fatigue, pain and discomfort, sleep and rest subscales), Psychological health (concerning bodily image and appearance, feelings, self-esteem, thinking, learning, memory and concentration subscales) and domains assessing overall QoL.

Poor QoL of caregiving mothers can be explained by guilt for having generated a child with genetically determined disease and anguish of impending dead for medical complications.

Quality of life in caregivers of children with sickle cell disease was found significantly lowered on all subscales if compared with a control group of the same socio-economic status by Questionnaire for Adult's Health-related Quality of Life. 18

Despite some limitations 19,20,21, our study is provocative and has potential implications for future research. It should be considered in the context of the following considerations:

1. endemic countries in the Mediterranean region, by long-established control programs have achieved 80-100% prevention of newly affected births, so the small sample size of present study reflects these strategies of prevention and avoiding the pregnancies in heterozygotic couple that have reduced dramatically incidence of β-thalassaemia major in Sicily;

2. we were aware that whole group of patients were psychologically stressed, therefore the choice to include all patients in the FCBT sessions was based on need to give support to all patients.
3. in order to assess the degree to which the effects of a sustainable psychological support could influence the lived experience of parenting a child with thalassaemia major, longitudinal study of changes over the life span of thalassaemic people should be necessary.

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Tab. 1 CBCL and MASC subitems (T-scores) in β-thalassaemic major children and in control subjects; mean ± SD.

<table>
<thead>
<tr>
<th>N. subjects</th>
<th>β-Thalassaemic children</th>
<th>Normal subjects</th>
<th>P</th>
</tr>
</thead>
<tbody>
<tr>
<td>CBCL</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Withdrawn</td>
<td>54.25±5.78</td>
<td>57.64±7.42</td>
<td>n.s.</td>
</tr>
<tr>
<td>Somatic complaints</td>
<td>58.29±7.37</td>
<td>53.32±4.48</td>
<td>&lt; .005</td>
</tr>
<tr>
<td>Anxious/depressed</td>
<td>54.57±5.41</td>
<td>56.54±7.71</td>
<td>n.s.</td>
</tr>
<tr>
<td>Social problems</td>
<td>55.11±7.12</td>
<td>56.61±7.67</td>
<td>n.s.</td>
</tr>
<tr>
<td>Thought problems</td>
<td>52.57±5.17</td>
<td>53.57±3.01</td>
<td>n.s.</td>
</tr>
<tr>
<td>Attention problems</td>
<td>53.71±5.35</td>
<td>55.21±5.91</td>
<td>n.s.</td>
</tr>
<tr>
<td>Delinquent behaviour</td>
<td>54.50±5.10</td>
<td>55.54±7.18</td>
<td>n.s.</td>
</tr>
<tr>
<td>Aggressive behaviour</td>
<td>52.86±3.94</td>
<td>54.43±6.57</td>
<td>n.s.</td>
</tr>
<tr>
<td>MASC</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Physical symptoms</td>
<td>48.79±6.37</td>
<td>45.04±3.52</td>
<td>&lt; .005</td>
</tr>
<tr>
<td>Harm avoidance</td>
<td>42.86±9.63</td>
<td>43.36±8.69</td>
<td>n.s.</td>
</tr>
<tr>
<td>Social anxiety</td>
<td>47.64±8.65</td>
<td>47.86±6.26</td>
<td>n.s.</td>
</tr>
<tr>
<td>Separation panic</td>
<td>53.36±10.31</td>
<td>48.18±6.96</td>
<td>&lt; .05</td>
</tr>
<tr>
<td>Anxiety disorders</td>
<td>41.29±9.19</td>
<td>40.75±6.54</td>
<td>n.s.</td>
</tr>
<tr>
<td>Total</td>
<td>48.00±8.75</td>
<td>44.32±5.16</td>
<td>n.s.</td>
</tr>
<tr>
<td>CDI</td>
<td>7.29±5.45</td>
<td>6.68±3.79</td>
<td>n.s.</td>
</tr>
</tbody>
</table>

Tab. 2. EAS in β-thalassaemic major children and their mothers and in healthy subjects; mean ± SD; number of cases in parenthesis.

<table>
<thead>
<tr>
<th>EAS for children</th>
<th>β-Thalassaemic patients (28)</th>
<th>Normal subjects (28)</th>
<th>P</th>
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</thead>
<tbody>
<tr>
<td>Emotionality</td>
<td>2.80±0.91</td>
<td>2.29±0.81</td>
<td>p &lt; .05</td>
</tr>
<tr>
<td>Activity</td>
<td>3.60±0.74</td>
<td>3.69±0.59</td>
<td>n.s.</td>
</tr>
<tr>
<td>Sociability</td>
<td>2.74±0.51</td>
<td>3.50±0.70</td>
<td>p &lt; .000</td>
</tr>
<tr>
<td>Shyness</td>
<td>2.60±0.75</td>
<td>2.34±0.49</td>
<td>n.s.</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>EAS for mothers</th>
<th></th>
<th></th>
<th>P</th>
</tr>
</thead>
<tbody>
<tr>
<td>Emotionality</td>
<td>2.98±0.71</td>
<td>2.40±0.28</td>
<td>p &lt; .000</td>
</tr>
<tr>
<td>Activity</td>
<td>3.19±0.61</td>
<td>3.25±0.45</td>
<td>n.s.</td>
</tr>
<tr>
<td>Sociability</td>
<td>3.45±0.52</td>
<td>4.13±0.59</td>
<td>p &lt; .000</td>
</tr>
<tr>
<td>Shyness</td>
<td>2.63±0.78</td>
<td>2.10±0.69</td>
<td>p &lt; .05</td>
</tr>
</tbody>
</table>
Tab. 3 WHOQOL-Bref in mothers with β-thalassaemic major children vs. normal group mothers; mean ± SD; number of cases in parenthesis. Higher scores indicate a higher QOL.

<table>
<thead>
<tr>
<th>Domains</th>
<th>Physical health</th>
<th>Psychologic health</th>
<th>Social relationships</th>
<th>Enviroment quality of life</th>
<th>General health</th>
</tr>
</thead>
<tbody>
<tr>
<td>β−thalassemia group mothers</td>
<td>57.29±11.47</td>
<td>63.80±9.22</td>
<td>74.01±14.25</td>
<td>48.54±14.41</td>
<td>62.50±15.96</td>
</tr>
<tr>
<td>(28)</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>58.04±19.31</td>
</tr>
<tr>
<td>Normal group mothers</td>
<td>68.45±15.68</td>
<td>69.59±7.43</td>
<td>79.37±10.01</td>
<td>50.85±1.47</td>
<td>77.98±13.75</td>
</tr>
<tr>
<td>(28)</td>
<td>p&lt; .005</td>
<td>p&lt; .05</td>
<td>n.s.</td>
<td>n.s.</td>
<td>p&lt; .000</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>p&lt; .05</td>
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